Implantation and Explantation of Active Subretinal Visual Prostheses Using a Combined Transcutaneous and Transchoroidal Approach

Florian Gekeler[1], Peter Szurman[1], Dorothea Besch[1], Martin Rohrbach[1], Eberhart Zrenner[1], Karl Ulrich Bartz-Schmidt[1], and Helmut Sachs[2]

With 5 Figures

Abstract

We are reporting on the surgical technique for implantation and explantation of subretinal visual implants with extra-ocular and extra-corporeal parts. We have thus far implanted 11 patients successfully. Visual percepts ranged from recognition of simple geometric forms up to letter recognition which technically was corresponded to a visual acuity of more than 0.02. Surgery was performed in all cases without complications. Histology showed that the implant is tolerated well. Future implants will have a prolonged implantation period and be wirelessly controlled.

Zusammenfassung

Wir berichten über die chirurgische Technik zur Implantation und Explantation von subretinalen Sehimplantaten mit extra-okularen und extra-korporalen Anteilen. Es wurden bisher 11 Patienten erfolgreich operiert. Die Seheindrücke schwankten zwischen der Wahrnehmung von einfachen geometrischen Formen bis hin zur Erkennung von Buchstaben, was rechnerisch einer Sehschärfe von über 0.02 entsprach. Die Chirurgie konnte in allen Fällen komplikationsfrei durchgeführt werden. Histologische Ergebnisse zeigen, dass das Implantat sehr gut toleriert wird. Künftige Implantate werden eine deutlich verlängerte Tragedauer haben und drahtlos gesteuert sein.

1. Introduction

Active subretinal implants receive energy from external sources to elicit visual perceptions by electrical stimulation of retinal cells (Rizzo et al. 2001, Zrenner 2002a). Since electrical energy from solely microphotodiode based is not sufficient (Stett et al. 1998, 1999, 2000), external energy is mandatory and has been supplied by a cable connection in our group recently (Besch et al. 2008, Gekeler et al. 2008, Zrenner et al. 2009). Retinal implants are primarily designed for patients suffering from degenerative retinal disease such as retinitis pigmentosa (RP) where outer retinal cells deteriorate while inner retinal cells stay intact a longer time (Santos et al. 1997, Stone et al. 1992) and can be used to transmit electronically generated signals to the brain.

---

1 Centre for Ophthalmology, University of Tübingen, Schleichstraße 12–16, 72076 Tübingen, Germany.
2 Klinikum Friedrichstadt, Dresden, Germany.

Implantation surgery has been described before for extra-ocular/orbital surgery (Besch et al. 2008, Gekeler et al. 2008) and vitreal surgery (Sachs et al. 2000, 2008, 2009). Here we are reporting on our experience in implantation surgery in 11 consecutive patients suffering from RP (Zrenner et al. 2009). Special attention is paid to the explantation procedure which was usually performed several months later as required by our local approval institutions. In light of recently reported adverse events where rapid explantation is required as well as in light of patients' requests for newer generation implants, in our opinion explantation has thus far been undervalued. This prompted us to investigate the explantation procedures in our patients who were implanted with an active subretinal prosthesis with a permanent extra-corporeal connection.

2. Material and Methods

2.1 Patients

We included 11 patients with end stage RP (10 males, 1 female). Remaining vision was required to be 'of no use in daily life'. In all subjects electrical excitability was ensured by prior trans-corneal electrical stimulation with DTL-electrodes (Gekeler et al. 2006c). All experiments were undertaken with the understanding and written consent of each subject respecting the Code of Ethics of the World Medical Association (Declaration of Helsinki) and in accordance with the European Communities Council Directive of November 24, 1986 (86/609/EEC). The study was approved by the local university's ethics committee which granted permission for a study period of 4 weeks in the first 8 patients and 4 months in the last 3 patients.

2.2 The Subretinal Prosthesis

The prosthesis consisted of four parts (Fig. 1).
– The subretinal part (*i*). – with (*a*) the MPDA with 1,550 photodiodes and titanium-nitride electrodes driven by light falling onto it through the optics of the eye and powered by external energy transferred via gold connection lanes on the polyimide foil strip, and (*b*) 16 titanium-nitride electrodes in a 4 × 4 array for direct, light independent, electrical stimulation; each electrode is connected to an outside stimulus generator via connection lanes on the trans-sclerally, trans-choroidally implanted foil strip.
– The extra-ocular part (*ii*). – After choroidal and scleral penetration the foil strip is flipped to lay episclerally. It then leads under the lid to the lateral orbital rim. For fixation, a patch of polytetrafluoroethylene glued to the foil is sutured onto the sclera. At the end of the foil strip a silicone patch is fixed by sutures in two holes through the lateral orbital rim.
– The subdermal part (*iii*). – The foil strip connects in the temporal fossa to a silicone cable with spirally twisted, isolated wires, which lead subperiostally beneath the temporal muscle to the retro-auricular space where it surfaces into a plug. There the device is fixed to the bone by a stainless steel clamp.
– An extra-corporeal part (*iv*). – The play connects to a stimulus generator.

Fig. 1   Photograph of the active subretinal implant. It consists of four parts: (*i*) The subretinal part (polyimide foil strip, 20 µm thick, 3.2 mm wide, approximately 22 mm long) with: a 4 × 4 array of titanium-nitride electrodes (diameter 50 µm, spacing 280 µm) and a microphotodiode array with 1,550 photodiodes and electrodes (electrode diameter 70 µm, spacing 70 µm, thickness 70 µm) which lies para-foveally. (*ii*) The extra-ocular part (polyimide foil) carrying 22 golden connection lanes to the external connection and the reference electrode. At length 12 and 26 mm from the tip two polytetrafluoroethylene pads are mounted for fixation on the sclera. At approximately 55 mm from the tip a silicone pad is glued to the polyimide foil for suture fixation to the lateral orbital rim. (*iii*) The subdermal part (silicone cable, diameter 3 mm) leads the connections on the polyimide foil to the external part by 22 spiraled gold flexes. The silicone cable perforates the retro-auricular skin. (*iv*) The external part consists of the silicone cable which connects via a plug to an external generator for control signals, energy, and stimuli.

2.3 Histology

Tissue samples surrounding the extra-corporeal implant were taken during explantation at various sites. Tissue was embedded in paraffin in the usual manner. 4−5 µm thick sections were stained with hematoxylin-eosin (H&E), Periodic acid Schiff (PAS), and Masson's trichrome. Moreover, various immunohistochemical stains like CD4, CD8, CD68, sm-actin, and KI67 and were performed.

3. Results

3.1 Implantation Surgery

The implantation procedure was carried out sequentially in the following steps as has been previously described in more detail (Fig. 2) (BESCH et al. 2008, GEKELER et al. 2008). In short, the skin was incised in the retro-auricular space. Approximately 2 cm by 2 cm of bone were exposed and two holes drilled to fix a metal clamp fixed with osteosynthesis screws. Then a prolonged brow incision was performed to expose the lateral orbital rim. Two holes were drilled 2 mm superior and inferior to the *sutura zygomatico-frontalis* and threads were inserted. Preparation proceeded laterally into the *fossa temporalis* elevating the temporalis muscle and the periosteum. From the subconjunctival space in the upper temporal quadrant a tunnel was bluntly prepared through the septum to the brow incision and was kept patent by a small silicone tube. A specially made trocar was advanced from the periorbital region subperiosteally until it reached the retroauricular area. The implant could then be advanced inside in anterior direction and the trocar removed leaving the implant in place. The intra-ocular surgery comprised a pars-plana-vitrectomy, creation of a subretinal bubble and trans-choroidal penetration in the upper lateral quadrant of the eye. Then, the fixation pad was sutured onto the sclera and the retina re-attached by perfluorocarbon liquids and filled with silicone oil for endotamponade.
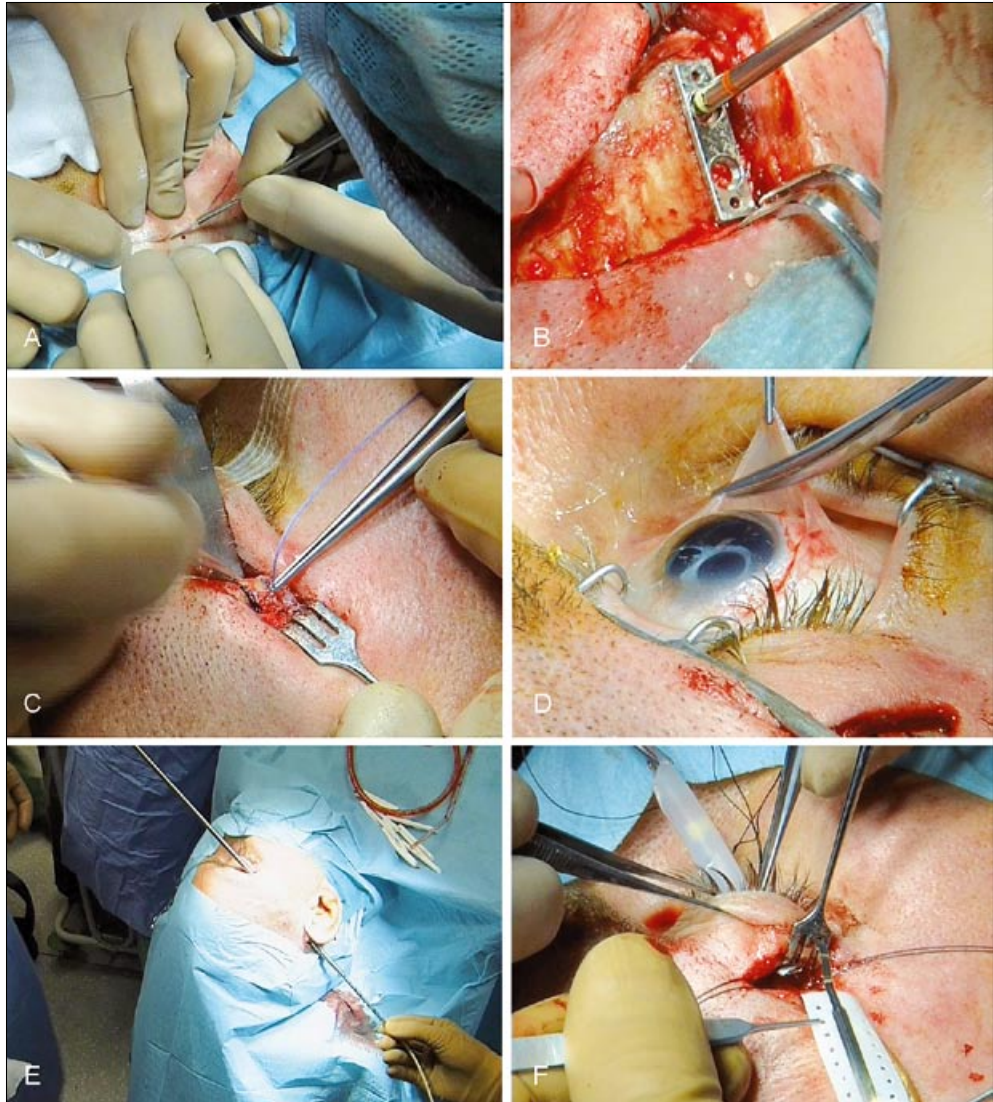
Fig. 2 Photographs of the decisive surgical steps for implantation. (*A*) Performing the retro-auricular cut. (*B*) Fixation of the base of the fixation clamp with two osteosynthesis screws. (*C*) Pulling threads through the two holes through the lateral orbital rim (2 mm above and below the *sutura zygomatico-frontalis*) for fixation of the implant. (*D*) Lifting the conjunctiva before the 360° incision. (*E*) Using the trocar in anterior-posterior direction in which the implant is inserted in opposite direction. (*F*) Insertion of the implant to the subconjunctival space.

The surgical procedure provided no major difficulties. The procedure of subperiostal implantation from the retro-auricular space to the orbital rim using the trocar proved to be well controllable in all cases. In general, the most challenging part was the protection of the implant during all steps of the surgery; touching the MPDA or the electrodes was not possible with any instrument and even fine threads could easily tear the polyimide foil and

lead to disruption of the gold wires (besides constituting a predetermined breaking point). Of this, an especially delicate part turned out to be pulling the polyimide foil with the sub-retinal parts through the opening from the lateral orbital rim under the lateral lid to the subconjunctival space. First, because the fairly large protecting silicone tube exerted considerable pressure onto the globe leading to a marked increase in intraocular pressure requiring fast maneuvers. Second, because the delicate subretinal parts had to be protected against mechanical injury by placement inside of the silicone tube while pulling the tube through the iatrogenic access. To facilitate this and provide better protection for the globe and the implant, a metal cartridge has been used in the last three patients. The cartridge was smaller in diameter, and a thread could be attached to pull it through the iatrogenic access (Fig. 1*F*); it considerably reduced pressure increases on the globe and helped to protect the implant's tip. Coagulation by monopolar or bipolar diathermia was to be avoided in the proximity of the implant because high-frequency electrical fields could damage the MPDA which acted as an antenna. To protect the implant a large spatula (touching the sclera to conduct any currents) was placed between it and the coagulating tip. During the following intra-ocular surgery the implants tip was kept away inside of the silicone/metal tube taped to the surgical drape.

In all 11 patients the implantation surgery, extra- as well as intra-ocular, could be performed as planned. No intra-operative complications were encountered. Surgery was performed in all cases without damaging the prosthesis. Figure 2 shows selected surgical steps in one patient. Time for extra-ocular surgery was 1.5 to 2.5 h; the whole surgery lasted 6 to 7 h.

3.2 Surgical Outcome

During the first postoperative days moderate edema and hematoma in the periorbital region were noticeable. The subdermal passage to the retro-auricular space proved to be unproblematic in all cases, leading to only minimal swelling and almost no pain. Two patients complained about a mild jaw closure blockade noticed during chewing which had disappeared one week postoperatively. A possible cause is an irritation of the temporal muscle or some fibers of the facial nerve in this region of the cable passage. Conjunctival chemosis and injection were observed in all patients comparable to other intraocular procedures such as pars-plana-vitrectomy. After approximately 5 days conjunctival chemosis, edema and hematomas had almost completely resolved and patients were discharged.

All wounds healed properly and no signs of infections or wound dehiscence were noticed. The skin penetration of the silicone cable proved to be well tolerable and unproblematic over the whole examination period.

Computed tomography scans of one patient and 3-dimensional reconstructions are shown in Figure 3.

The retina was attached immediately post-operatively until explantation in all cases. In the early postoperative days some retinal edema over the MPDA was present in optical coherence tomography. The amount of edema decreased during the first post-operative week. Fluorescein angiography could show capillaries in fine detail over the MPDA because the opaque MPDA totally blocked background fluorescence from the choroid. In the periphery (upper temporal part) of the MPDA capillary rarefication was noticeable, which could either be due to mechanical obstruction from the thickness of the soldering points of the MPDA in this region or due to pre-existent changes in RP retinas (GEKELER et al. 2007).

Fig. 3   3D reconstruction of computed tomography scans of one patient approximately 2 years after implanta-
tion. (*A*) Side view of the reconstruction which shows the path of the silicone cable from the retro-auricular re-
gion through the temporal fossa around the lateral orbital rim. The ticker part in the temporal fossa is the transi-
tion from the silicone cable to the polyimide foil. (*B*) Frontal view showing the polyimide foil within in the orbit,
the episcleral part and the subretinal part where the thicker ending of the implant constitutes the microphoto-
diode array and the direct stimulation electrodes.

3.3 Explantation Surgery

First, the skin was re-opened in the retro-auricular space and in the brow region pos-
teriorly to the temporal fossa. The implant was then carefully exposed by blunt prepa-
ration. Especially under the conjunctiva there was considerable scar tissue which had
formed around the implant. This tissue, however, was not adherent to the implant's
structures, but rather formed a capsule in which the implant could slide. Then the sili-
cone cable was dissected at the junction with the polyimide foil in the temporal fossa.
The screws of the clamp in the retro-auricular space were removed and the silicone ca-
ble pulled posteriorly which posed almost no measurable resistance due to the capsule
also found in this region. The basal plate of the clamp and the bone screws were re-
moved and the skin closed again. Following that intra-ocular parts of the implant were
removed by loosening the scleral fixation pad and the scleral access was re-opened
to pull out the intra-ocular parts. No intra-ocular procedure was required. All wounds
were finally closed in layers. Silicone oil was removed approximately 3 months later,
depending on the individual situation. Several steps of explantation surgery are shown
in Figure 4.

Prostheses were explanted after 4 weeks in patients 2, 3, and 4; and after 5 weeks in
patients 5, 6, and 7. The elongation of the study period was permitted by the local ethics
committee. Patient 1 refused to have the device explanted.

At explantation the implant was surrounded by scar tissue, which was – due to the
inert nature of the polyimide, silicone, and expanded polytetrafluoroethylene materials
– not connected to any of the implant's parts. Therefore, after careful dissection of this
tissue using microsciscors and removal of episcleral and bone sutures the device could
simply be pulled out as described above. Explantation was uneventful in all 6 cases and
patients could be discharged on the following day.

3.4 Functional Results

Eight patients reported topical correct visual percepts by the direct stimulation array and 6 patients also by light stimulation through the MPDA (ZRENNER et al. 2006, 2009). Details will be published in upcoming publications.

3.5 Histology

Histology showed the formation of scar tissue (condensed connective tissue) along the extra-corporeal implant as a morphological correlate of the described capsule. Fibroblasts invaded the polytetrafluoroethylene pad covering the polyimide foil. There was a moderate inflammatory reaction consisting of CD4, CD8, and especially CD68 positive cells along the extra-bulbar implant. Foreign body giant cells were primarily seen in the vicinity of the polytetrafluoroethylene pad (Fig. 5).

4. Discussion

We have developed a surgical procedure that allows safe implantation and explantation of active visual prostheses with extra-corporeal parts. The study in 11 patients has proven that the surgical access is feasible for a period of at least four weeks. Surgery was successful in all cases and lead to stable placement of the prosthesis. No postoperative complications were encountered, such as infections or displacement of implants. Patients altogether felt astonishingly little irritation from the surgical procedure and the presence of the device. The trans-cutaneous connection proved to be uncomplicated and usable for repeated connection and disconnection of the stimulator.

Since in previous animal experiments small dislocations of the implant's subretinal parts have lead to retinal tears and retinal detachments (GEKELER et al. 2006b), multiple tension relief points were introduced along the course of the implant: flexible pads for fixation on the sclera, two sutures through holes in the bone of the lateral orbital rim, and by a metal clamp on the scull bone in the retro-auricular space for the silicone cable. Consequently, no retinal detachments or dislocations were noticed.

Explantation was required in our case by local ethics committee after 4 weeks in the first 8 patients and after 4 months in the three last patients. However, there are several more situations when explantation is required, such as major complications (e. g. endophthalmitis has been reported by other groups; HUMAYUN 2009) or when patients request more up-to-date implants. Therefore, the finding that explantation of devices with extra-ocular parts (which most groups now favor) is feasible is of great value. Explantation surgery required extra attention due the scar tissue found especially in the subconjunctival space, but was successful in all cases and implants were available for further technical examination. The implant itself was not connected to any tissue due to the inert materials used (polyimide, titanium, silicone).

Histology showed the usual condensation of connective tissue at the host tissue-implant interface. Inflammation was generally moderate but recognizable with a foreign body reaction (giant cells) especially in the vicinity of the polytetrafluoroethylene pad and polyimide foil.
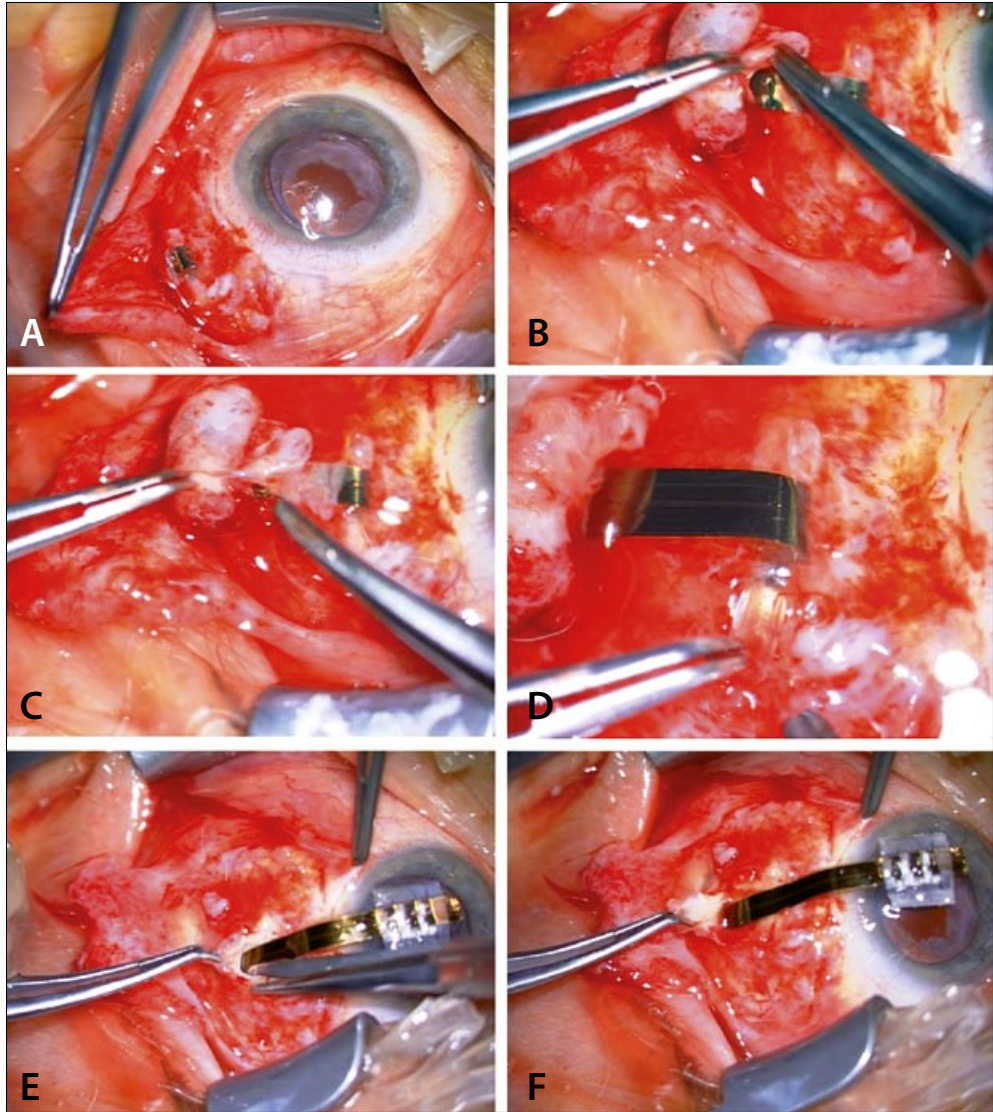
Fig. 4   Photographs of the decisive steps for explantation. (*A*) The polyimide foil can be seen after lifting the conjunctiva in the upper temporal quadrant of the left eye of this patient after 3 months. (*B*) and (*C*) The foil is surrounded, but not adherent to scar tissue which produces a kind of capsule that is incised carefully. (*D*) Removal of the artificial hypomochlion made from silastic tubing that was placed to protect the foil from potential damage of sharp bends. (*E*) The scar tissue is opened more posteriorly. (*F*) The original scleral flap is prepared (lifted up here by the forceps).

As a first step in this study, an extra-corporeal connector was used through a trans-cutaneous cable in order to be able to directly measure charge transfer and impedance of individual electrodes. Using a direct connection we were also able to optimize the control settings for the MPDA, which will be used for the next implantations with a wirelessly controlled implant. An extra-corporeal connection does certainly not qualify for permanent and rou-
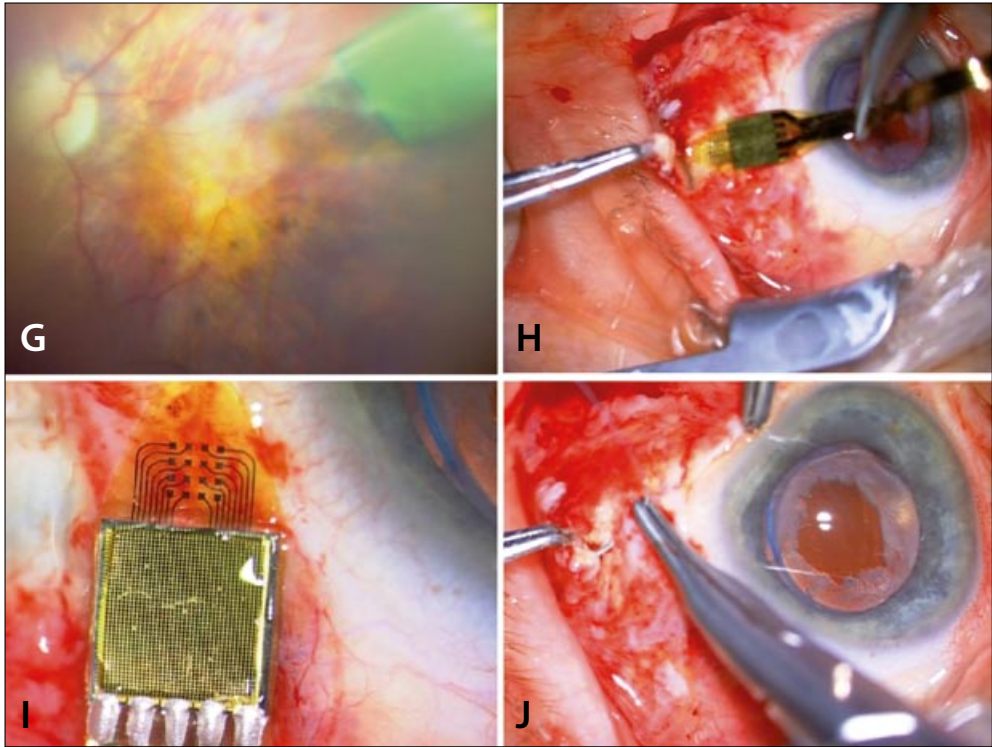
Fig. 4 (*G*) Fundus view (taken through the operating microscope) showing the implant already partially removed, which leaves a depigmented area in the original place. (*H*) The implant can simply be retracted with silicone oil in place. (*I*) A first glimpse at the implant after explantation under the microscope reveals completely intact structures: 16 direct stimulation electrodes at the top and the microphotodiode array with approximately 1,600 diodes on the bottom. (*J*) Suturing of the scleral flap for globe closure.

tine use. We feel, however, that this step was justified in regard of the very positive results of the study and the low complication rate.

Other groups have already placed wireless systems either in the retro-auricular space (HUMAYUN et al. 2003), episclerally (RIZZO et al. 2008), or even intra-ocularly as a modified intra-ocular lens in the capsular bag (ALTEHELD et al. 2007). A totally intra-ocularly implantable device is still, even when using up-to-date technology, large in size and the trauma inferred for implantation is considerable since it requires a large limbal opening and combined anterior and posterior segment surgery with a wired connection e. g. from the capsular bag to the episcleral surface (ALTEHELD et al. 2007), or possibly even to the subretinal space. The easier surgical access and the additional room in the extra-ocular space give more freedom in the choice of the receiver coils and control circuitry. In our opinion therefore, a system where the receiver and control units of a wireless system are placed extra-ocularly bears significant advantages. In particular, in regard of the unproblematic trans-choroidal, trans-scleral penetration with a wired connection in our cases and in the literature (BESCH et al. 2008, GEKELER et al. 2006a, 2007, SACHS et al. 2005, HUMAYUN et al. 2003) a completely intra-ocularly implantable system does not seem essential. Several steps of the extra-ocular surgery presented in our study can contribute to implan-
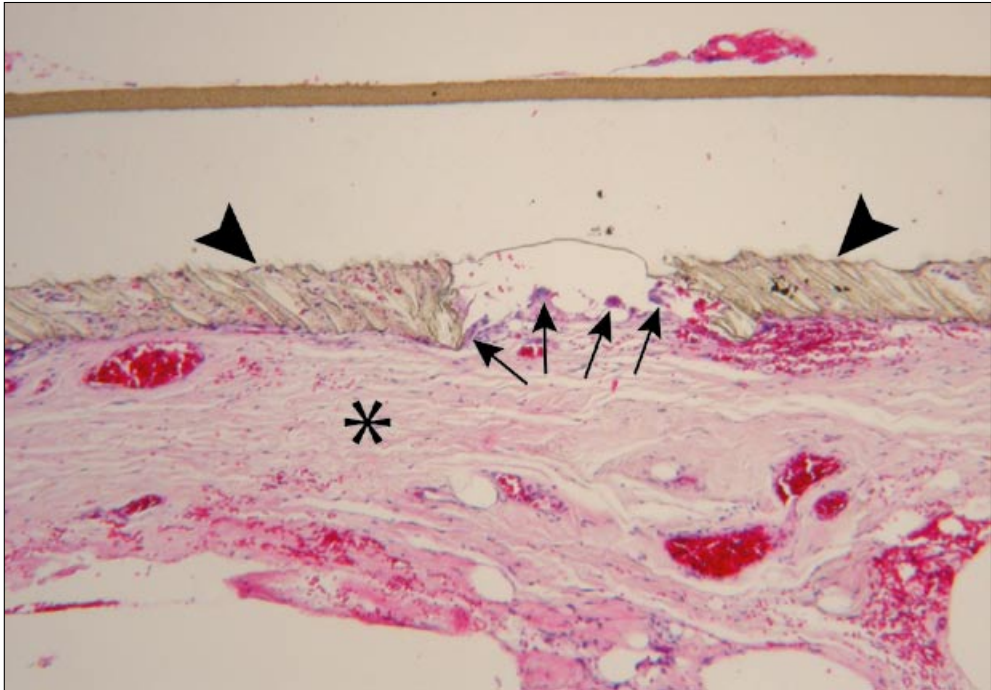
Fig. 5   Histological section of tissue surrounding the implant (polytetrafluoroethylene pad polyimide foil) taken at the time of explantation after approximately 2 months. Fibroblasts have invaded the porous polytetrafluoroethylene pad patch (arrow heads) which is lined by foreign body giant cells (arrows). Connective tissue seems condensed besides the implant (asterisk) with mainly longitudinal orientation of the collagen fibers (H&E).

tation of such a prosthesis and also under other circumstances in ophthalmic research, e. g. when intra-ocular technical devices have to receive or transmit signals, such as intra-ocular pressure (e. g. WALTER et al. 2000) or temperature sensors (e. g. SAILER et al. 2007), epi- or sub-retinal prostheses, and also optic nerve head prosthesis (in RIZZO et al. 2001, ZRENNER 2002 b).

In conclusion, our study in eleven patients has proven the feasibility of a trans-cutaneous, trans-choroidal cable connection to the subretinal space using the described surgical procedure. Implantation and explantation were highly successful and led to stable placement in all cases. Functional results are extremely promising (ZRENNER et al. 2009).

References

ALTEHELD, N., ROESSLER, G., and WALTER, P.: Towards the bionic eye-the retina implant: surgical, opthalmological and histopathological perspectives. Acta Neurochir. Suppl. *97*, 487–493 (2007)

BESCH, D., SACHS, H., SZURMAN, P., GULICHER, D., WILKE, R., REINERT, S., ZRENNER, E., BARTZ-SCHMIDT, K. U., and GEKELER, F.: Extraocular surgery for implantation of an active subretinal visual prosthesis with external connections: feasibility and outcome in seven patients. Br. J. Ophthalmol. *92*, 1361–1368 (2008)

GEKELER, F., MESSIAS, A., OTTINGER, M., BARTZ-SCHMIDT, K. U., and ZRENNER, E.: Phosphenes electrically evoked with DTL electrodes: a study in patients with retinitis pigmentosa, glaucoma, and homonymous visual field loss and normal subjects. Invest. Ophthalmol. Vis. Sci. *47*, 4966–4974 (2006a)

GEKELER, F., MESSIAS, A., OTTINGER, M., BARTZ-SCHMIDT, K. U., and ZRENNER, E.: Phosphenes electrically evoked with DTL electrodes: a study in patients with retinitis pigmentosa, glaucoma, and homonymous visual field loss and normal subjects. Invest. Ophthalmol. Vis. Sci. *47*, 4966–4974 (2006b)

GEKELER, F., OTTINGER, M., MESSIAS, A., and ZRENNER, E.: Phosphenes from electrical stimulation with DTL-electrodes in various retinal diseases: Chronaxie and rheobase. Invest. Ophthalmol. Vis. Sci. *47*/11, 4966–4974 (2006c)

GEKELER, F., SACHS, H., SZURMAN, P., GUELICHER, D., WILKE, R., REINERT, S., ZRENNER, E., BARTZ-SCHMIDT, K., and BESCH, D.: Surgical procedure for subretinal implants with external connections: The extra-ocular surgery in eight patients. Invest. Ophthalmol. Vis. Sci. *49*, 4049 (2008)

GEKELER, F., SACHS, H., SZURMAN, P., MESSIAS, A., WILKE, R., BESCH, D., WILHELM, B., ZRENNER, E., BARTZ-SCHMIDT, K., and GELISKEN, F.: Fluorescein angiographic findings in blind patients treated by an active subretinal implant. Invest. Ophthalmol. Vis. Sci. *48*, 2567 (2007)

GEKELER, F., SZURMAN, P., GRISANTI, S., WEILER, U., CLAUS, R., GREINER, T. O., VOLKER, M., KOHLER, K., ZRENNER, E., and BARTZ-SCHMIDT, K. U.: Compound subretinal prostheses with extra-ocular parts designed for human trials: successful long-term implantation in pigs. Graefe's Arch. Clin. Exp. Ophthalmol. *245*/2, 230–241 (2007)

HUMAYUN, M. S.: Preliminary results from Argus II Feasibility Study: A 60 electrode epiretinal prosthesis. Invest. Ophthalmol. Vis. Sci. *50*, 4744 (2009)

HUMAYUN, M. S., WEILAND, J. D., FUJII, G. Y., GREENBERG, R., WILLIAMSON, R., LITTLE, J., MECH, B., CIMMARUSTI, V., van BOEMEL, G., DAGNELIE, G., and DE JUAN, E.: Visual perception in a blind subject with a chronic microelectronic retinal prosthesis. Vision Res. *43*, 2573–2581 (2003)

RIZZO, J. F. III, CHEN, J., SHIRE, D., KELLY, S., GINGERICH, M., SWIDER, G., DROHAN, W., and WYATT, J. L.: Implantation of a wirelessly powered retinal prosthesis using an ab externo surgical technique. Invest. Ophthalmol. Vis. Sci. *49*, 3027 (2008)

RIZZO, J. F. III, WYATT, J., HUMAYUN, M., DE JUAN, E., LIU, W., CHOW, A., ECKMILLER, R., ZRENNER, E., YAGI, T., and ABRAMS, G.: Retinal prosthesis: An encouraging first decade with major challenges ahead. Ophthalmology *108*, 13–14 (2001)

SACHS, H. G., BARTZ-SCHMIDT, U., GEKELER, F., BESCH, D., BRUNNER, U., WILHELM, B., WROBEL, W., WILKE, R., GABEL, V.-P., and ZRENNER, E.: The transchoroidal implantation of subretinal active micro-photodiode arrays in blind patients: Long term surgical results in the first 11 implanted patients demonstrating the potential and safety of this new complex surgical procedure that allows restoration of useful visual percepts. Invest. Ophthalmol. Vis. Sci. *50*, 4742 (2009)

SACHS, H. G., BRUNNER, U., GEKELER, F., BARTZ-SCHMIDT, K.-U., GABEL, V.-P., WROBEL, W., HEKMAT, A., and ZRENNER, E.: The development of a guiding tool for transchoroidal subretinal chip implantation to protect the retina. Invest. Ophthalmol. Vis. Sci. *49*, 4045 (2008)

SACHS, H. G., KOBUCH, K., KÖHLER, M., SCHWAHN, H. N., GEKELER, F., JAKOB, W., MARIENHAGEN, J., GABEL, V. P., and ZRENNER, E.: Subretinal implantation of electrodes for acute stimulation of the retina to evoke cortical responses in minipig. Invest. Ophthalmol. Vis. Sci. *41*, S102 (2000)

SACHS, H., SCHANZE, T., FRAMME, C., GEKELER, F., WILMS, M., BRUNNER, U., NISCH, W., SAILER, H., ZRENNER, E., and GABEL, V. P.: The evaluation of subretinal stimulation by film-electrode arrays suitable for chronic human experiments in animal models. Invest. Ophthalmol. Vis. Sci., Annual Meeting 2004, Abstract 4206 (2005)

SAILER, H., SHINODA, K., BLATSIOS, G., KOHLER, K., BONDZIO, L., ZRENNER, E., and GEKELER, F.: Investigation of thermal effects of infrared lasers on the rabbit retina: a study in the course of the development of an active subretinal prosthesis. Graefe's Arch. Clin. Exp. Ophthalmol. *245*/8, 1169–1178 (2007)

SANTOS, A., HUMAYUN, M. S., DE JUAN, E., Jr., GREENBURG, R. J., MARSH, M. J., KLOCK, I. B., and MILAM, A. H.: Preservation of the inner retina in retinitis pigmentosa. A morphometric analysis. Arch. Ophthalmol. *115*, 511–515 (1997)

STETT, A., BARTH, W., WEISS, S., HAEMMERLE, H., and ZRENNER, E.: Electrical multisite stimulation of the isolated chicken retina. Vision Res. *40*, 1785–1795 (2000)

STETT, A., KOHLER, K., WEISS, S., HAEMMERLE, H., and ZRENNER, E.: Electrical stimulation of degenerated retina of RCS rats by distally applied spatial voltage patterns. Invest. Ophthalmol. Vis. Sci. *39*, Abstract 902 (1998)

STETT, A., TEPFENHART, M., KOHLER, K., NUESSLIN, F., HAEMMERLE, H., and ZRENNER, E.: Charge sensitivity of electrically stimulated chicken and RCS rat retinae. Invest. Ophthalmol. Vis. Sci. *40*, S734 (1999)

STONE, J. L., BARLOW, W. E., HUMAYUN, M. S., DE JUAN, E., Jr., and MILAM, A. H.: Morphometric analysis of macular photoreceptors and ganglion cells in retinas with retinitis pigmentosa. Arch. Ophthalmol. *110*, 1634–1639 (1992)

Florian Gekeler et al.

Walter, P., Schnakenberg, U., vom Bögel, G., Ruokonen, P., Kruger, C., Dinslage, S., Ludtke Handjery, H. C., Richter, H., Mokwa, W., Diestelhorst, M., and Krieglstein, G. K.: Development of a completely encapsulated intraocular pressure sensor. Ophthalmic Res. *32*, 278–284 (2000)

Zrenner, E.: The subretinal implant: Can microphotodiode arrays replace degenerated retinal photoreceptors to restore vision? Ophthalmologica *216*, 8–20 (2002a)

Zrenner, E.: Will retinal implants restore vision? Science *295*, 1022–1025 (2002b)

Zrenner, E., Besch, D., Bartz-Schmidt, K. U., Gekeler, F., Gabel, V. P., Kuttenkeuler, C., Sachs, H., Sailer, H., Wilhelm, B., and Wilke, R.: Subretinal chronic multi-electrode arrays implanted in blind patients. ARVO Meeting Abstracts 2004 (2006)

Zrenner, E., Wilke, R., Bartz-Schmidt, K., Benav, H., Besch, D., Gekeler, F., Koch, J., Porubska, K., Sachs, H., and Wilhelm, B.: Blind retinitis pigmentosa patients can read letters and recognize the direction of fine stripe patterns with subretinal electronic implants. Invest. Ophthalmol. Vis. Sci. *50*, 4581 (2009)

PD Dr. Florian Gekeler
Centre for Ophthalmology
University of Tübingen
Schleichstraße 12–16
72076 Tübingen
Germany
Phone: +49 70 71 2 98 47 61
Fax: +49 70 71 29 50 38
E-Mail: gekeler@uni-tuebingen.de